

which the drugs have to act in an environment in which host defenses are suboptimal. For example, surface phagocytosis probably does not occur in the relatively acellular vegetation.

In such a setting, it may also be useful to extend the definition of synergism to the concept that although one drug may be useful, the addition of a second agent may make the combination even more effective. It has been shown in experimental *Streptococcus viridans* endocarditis, for example, that the combination of penicillin G and streptomycin achieved cures more rapidly than penicillin alone⁷ even though the infecting organism was exceedingly sensitive to penicillin. Translated to the clinical situation, this may mean that patients with *Streptococcus viridans* subacute bacterial endocarditis (SBE) treated with a combination of penicillin and streptomycin may require only two weeks of parenteral therapy, compared with the customary four-week course that is employed with penicillin. There is suggestive evidence that this is the case,⁸ and if these observations are confirmed in a larger series of patients, the reduction in length of stay in hospital and its attendant costs would be significant.

It is, of course, tempting to extend these observations to other clinical situations in which host defenses have been compromised—such as a immunosuppressed, neutropenic host with malignant disease, who is so susceptible to infection particularly with Gram negative bacteria. However, here the data are equivocal. For example, a recent clinical trial indicated that the combination of cephalothin-carbenicillin-gentamicin was no better than cephalothin-carbenicillin given alone.⁹ Before proposing that a combination of antimicrobials will act synergistically, three criteria should be fulfilled: (1) the drugs must show synergism against the putative pathogen *in vitro*; (2) if possible, synergism must be shown in an experimental infection akin to the infection in man, and (3) the combination must be tested in man in a controlled clinical trial. Within the constraints of these criteria, it seems useful to investigate combinations of drugs against those organisms that continue to pose a hazard of life-threatening infection. However, until synergism can be shown for a combination, the better part of valor is to use only those agents to which the organisms clearly have been shown to be sensitive. Moreover, where possible these drugs should be used singly rather than in combination. Finally, when combination agents are used they

need to be deployed as single agents rather than as a single preparation in fixed combination.

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Editorial Essay

On the Withholding of Physicians' Services

FOR MORE than a decade practicing physicians have experienced a growing sense of frustration and with it growing resentment. Not only have there been mounting costs in patient care and clearly discriminatory cost controls against physicians, but worse, there has been increasing interference with medical practice by those who assume some authority but take no responsibility for what is or is not done for a patient who may be sick, injured or unable to cope for whatever reason. The root causes have been both economic and political.

First it was "third parties" in the private sector, and then government. Both have been guilty of discriminatory actions against physicians and both have built up large bureaucracies against whose medical practice decisions a practicing physician is virtually powerless—unless he wishes to invest a substantial amount of time and energy in making his case each time he differs with a bureaucratic decision. And most recently the

courts have decided to bring medical practice and medical practitioners to account under rules which may be appropriate enough for the legal system, but which affect medical practice and patient care adversely by making patients potential adversaries of their physicians. This fosters the development of wary doctor-patient relationships and the unwholesome practice of defensive medicine—which is always costly and seldom necessary or even best for the patient.

All of this has been frustrating, and as frustration mounts there is an understandable search for some force which can be brought to bear quickly and with effect. In our society, labor unions have developed such a force—though critics contend it has been done at some considerable cost to the freedom of their members and the public. The ultimate force that labor unions use is the strike, and to use this force effectively the union must be prepared to carry it on until the hurt it causes becomes intolerable to the employer, the public, or both. Unless this capability to hurt is real and there is willingness to use it, a strike method will not work.

The union idea has become attractive to many physicians in the same way it has been attractive to other groups of people who have been discriminated against or whose working conditions have been less than satisfactory. Further, those younger physicians, interns and residents in training, have shown that for them it can produce results. But it is worth remembering that, unlike most practicing physicians, interns and residents are in an employee status and also that their cause has had some emotional appeal to the public. They were serving the poor, they were television heroes, and their working conditions aroused sympathy. It is also worth noting that their protest was most effective when they did the opposite of withholding care—when they admitted everyone who needed care to the hospital and simply failed to discharge anyone. This was a quite different situation from that in which most practicing physicians now find themselves.

It seems to be becoming clear that the mass withholding of physicians' services is something to be feared by all concerned: profession, patients and general public. For the profession it flies in the face of the image and tradition of selfless service to the sick and injured. There is real danger that the profession will be viewed as self-serving at the expense of patients and the public. Physicians are not a deprived segment of society

—often overworked, yes, but not deprived. There is usually no great public sympathy for the plight of physicians except as patients and patient care are affected, for better or worse. For an ill patient there is real fear: "Will my doctor be willing to help me when I need him?" or "Will I be able to get any care at all?" For the public there not only is this same kind of fear, but also the fear created by any strike that threatens the public safety, such as by a strike of the police or firemen. For reasons such as these it seems unlikely that a strike by physicians could have much public support for very long.

The recent experience in Northern California is perhaps worth noting. When the professional liability insurance premiums of some four thousand doctors were abruptly doubled or tripled this acutely affected several specialties including anesthesiology. All but a few anesthesiologists felt that they should not have to meet these costs and pass them on to their patients, and more or less in unison most withdrew their services. There was substantial support for their position from physicians in other specialties and in other as yet unaffected parts of the state. Initially the public sensed injustice and there was considerable public support for the doctors. But when a number of community hospitals began to be seriously hurt financially, and needed patient care was being deferred, and the California legislature indicated an intention to deal with the problem in the current session, there was an abrupt reversal of public support for the further withholding of services. The anesthesiologists wisely decided to return to work even though many of their number wanted to remain "out" until legislation satisfactory to them was indeed enacted. There could be lessons to be learned from this experience.

These are perilous days for medicine in this nation. In history, there have been times when physicians were slaves and other times when they were honored and respected leaders of the tribe. In whatever role, physicians have always been essential and have served in accordance with the will of society. While it is not likely that physicians will be actually enslaved in today's society, nevertheless it is true that the shackles of governmental controls are beginning to be felt by every practicing physician as they begin to restrict his freedom to exercise his best judgment in caring for his patients. And there is reason to believe that Congress may soon enact a law which will actually indenture young physicians for a period

of involuntary service. The trend is clearly toward greater public control both of physicians and the medicine they practice.

It is well to ask, then, does medicine have any real social, economic or political strength that it can bring to bear in these critical times—and if so where does it lie? It is certainly not at the ballot box. Physicians have only one vote in a thousand and legislators know this. It is not in the physicians' pocketbooks, although these have to be tapped to achieve a variety of professional goals. And it is clearly not in the profession's ability to cause suffering or hurt—or even unnecessary inconveniences—to the sick or injured. Rather the strength of medicine lies in the opposite of these. It lies in first earning and then mobilizing the vigorous support of patients and the general public for its goals. This can amount to an enormous power, far surpassing any power the profession can hope to generate within itself.

It needs to be cultivated continually, in times of stress as well as in times less stressful, so that it can be brought to bear when needed.

These are times for the profession to keep its head—and for physicians to keep their cool. The role to be sought in society is that of wise and respected leadership, and the power to be mobilized is that of public understanding and support. The test for every action of every physician, of every group of physicians and of the profession itself is whether or not that action is best for patients and, therefore, for the public generally. It will always be true that what is best for patients is in the long run best for the medical profession. If the withholding of physicians' services can be justified by this test, then well and good. But there can be no doubt that the withholding of physicians' services can be a double-edged sword, and one edge could turn out to be quite a lot sharper than the other.

—MSMW

“Myasthenia Gravis”

Or the Autoimmunity, Thymic Disease, Neuromuscular Block Poser

MYASTHENIA GRAVIS is a disease that presents clinically with the symptoms of a postsynaptic neuromuscular block; the question arises—What causes this neuromuscular block? Two major clues loom large, thymic disease and autoimmunity; relating these to each other and to the neuromuscular deficit provides the poser of myasthenia gravis.

Thymic disease is consistently present in myasthenia gravis. In 15 percent of cases there is thymoma and in the remaining cases infiltration of thymus with lymphocytes and plasma cells and lymphoid germinal centers (these histological changes are also found in the nontumorous thymus adjacent to thymoma in myasthenia gravis). The nontumorous thymus in myasthenia gravis is, by common usage, termed hyperplastic but since the weight falls within the normal range this term is probably incorrect; the histological changes are more consistent with thymitis. The other important point to note with respect to the thymus in myasthenia gravis is that thymectomy, on an empirical basis, has been shown to cure or produce a substantial remission in up to 80 percent of cases. Failure to respond to thymectomy can

be attributed in most cases to ectopic thymic tissue, incomplete thymectomy or irreversible neuromuscular damage with long-standing disease.

Autoimmunity was first suggested in myasthenia gravis in 1960 and since that time this concept has been amply substantiated. There is extensive serological evidence of antibodies to a variety of self antigens and other corroborative evidence, including clinical and serological overlap with other autoimmune diseases and a predominance of certain histocompatibility antigen types probably related to the presence of certain immune regulation genes. The real question seems to be not Is there an autoimmune reaction? but rather How does an autoimmune reaction cause neuromuscular block?

Direct blockade of transmission by autoantibodies to the acetylcholine receptor sites is the concept that most people would regard as implicit when autoimmunity is broached in myasthenia gravis. This pathogenesis is supported by the finding that immunization of animals with purified acetylcholine receptors from electric eels results in autoantibodies to endogenous acetylcholine receptors which cause a postsynaptic lesion in the recipient and also produce an acute curare-like neuromuscular block when applied to a neuromuscular preparation *in vitro*.^{1,2} More recently, autoantibodies to acetylcholine receptor proteins have been detected in the serum of patients with